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GUIDELINES

Consensus of the French Society of Gerontology and Geriatrics and the French Society of Cardiology for the management of coronary artery disease in older adults

Consensus d'experts de la Société française de gériatrie et gérontologie (SFGG) et de la Société française de cardiologie (SFC) sur la prise en charge de la maladie coronaire chez le sujet âgé

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Summary Coronary heart disease is a common and serious condition in patients aged over 80 years. The presenting clinical symptoms are all the more atypical and the prognosis poorer when it occurs in patients with multiple comorbid diseases. The presence of comorbidities dictates the need for a standardized geriatric assessment to screen for the existence of underlying

Abbreviations: ACS, acute coronary syndrome; ADL, activities of daily living; ARA, angiotensin II receptor antagonist; ASSENT-3, Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention; CURE, Clopidogrel in Unstable angina to prevent Recurrent Events; GDS, geriatric depression scale; ECG, electrocardiogram; GISSI-3, Third Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico; HYVET, hypertension in the very elderly trial; IADL, instrumental activities of daily living; IONA, economic evaluation of the impact of nicorandil in angina; LMWH, low-molecular-weight heparin; MMSE, Mini Mental Status Examination; MNA, Mini Nutritional Assessment; PROSPER, pravastatin in elderly individuals at risk of vascular disease; PTCA, percutaneous transluminal coronary angioplasty; SCGA, standardized comprehensive geriatric assessment; SHOCK, SHould we emergently revascularize Occluded coronaries for Cardiogenic shocK?.

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frailty. The available scientific data were obtained during studies that included few subjects aged over 80 years. These recommendations are therefore mainly extrapolated from results obtained in younger populations. The pharmacological management and revascularization strategy for coronary heart disease in octogenarians is basically the same as in younger subjects. Epidemiological studies all concur that available therapies are underutilized despite the fact that this population has a high cardiovascular risk. Specific precautions for use must be respected because of the comorbidities and age-related changes in pharmacokinetics or pharmacodynamics. Generally, the therapeutic strategy in coronary heart disease is based not on the patient's real age, but rather on an individual analysis taking into account the severity of the coronary disease, comorbidities, the risk of drug misadventures, patient life expectancy and quality of life.

Introduction

Mortality due to ischaemic heart disease fell by 16% in France between 1988—1990 and 1995—1997, but this condition still causes 27% of deaths from cardiovascular disease. This mortality increases with age and is always higher in men [1]. Nearly one-third [2—4] of patients admitted for myocardial infarction are over 75 years old and represent nearly 50% of hospital mortality due to this disease. Patients over 85 years have six times more cardiogenic shocks, three times more strokes, twice as many major bleeding events and three to nine times higher mortality [5,6].

Few data are available in the literature about coronary insufficiency in adults aged over 80 years. Old age is an exclusion criterion in most randomized controlled trials on ACS. This article, compiled from a review of the literature, is an 'expert consensus' of the French Societies of cardiology and geriatrics/gerontology on the specific features of management of coronary heart disease in patients aged over 80.

Clinical approach

The presentation of coronary insufficiency in the older subject often differs from that in younger adults and atypical clinical features are often observed.

Angina pain

Angina pain remains the most frequent inaugural sign of coronary insufficiency in the elderly, although it has a lower incidence than in younger adults. It may be more difficult to analyse because of communication difficulties and in particular the presence of cognitive impairment, which may cause patients to 'forget' symptoms. Atypical pathological features are frequent in older adults, particularly in women: gastrointestinal disorders, asthenia and deterioration in general health status may be the main presenting symptoms. Ischaemic heart disease may also lead to blockpnea, acute pulmonary oedema, rhythm disorders or even sudden death [7].

Silent ischaemia

Silent ischaemia is more frequent in the elderly [8] because of impaired sensory nerve function, deterioration in cortical function or dysautonomia. Coronary heart disease may be asymptomatic when physical activity is reduced below the ischaemic threshold by a sedentary lifestyle or locomotor disability. The incidence of confounding diseases [9] (spondylosis or shoulder osteoarthritis, chest wall pain or gastrointestinal diseases) makes clinical analysis more difficult.

Myocardial infarction

Diagnosis of myocardial infarction may also be difficult in older adults and the presenting symptom may be a complication (acute pulmonary oedema, stroke, acute ischaemia of the lower limbs, heart rhythm disorder or sudden death) or a gastrointestinal or neurological symptom (confusional syndrome, behavioural disorders, syncope or vertigo or even simple headaches [10]). Atypical symptoms often lead to delays in treatment [11].

Clinical examination

The clinical examination determines the distribution of the atheromatous disease (arterial murmur, detection of abdominal aortic aneurysm). The physical examination may also reveal arrhythmia or signs of heart failure. A measurement of seated and then standing blood pressure is indicated (to test for orthostatic hypotension, defined as a fall of 20 mmHg in systolic blood pressure and/or 10 mmHg in diastolic blood pressure). Finally, a precise neurological examination should be performed. This should be completed by a SCGA.

Geriatric approach

The management of older adults with coronary insufficiency has different objectives depending on the patient. In autonomous elderly subjects with no severe concomitant disease, it is identical to that of younger adults. The aim of management of a dependent older adult with multiple comorbid diseases is to preserve vital functions while avoiding adverse drug reactions.

Global assessment

This essential assessment is often difficult to perform in an emergency setting and must be completed when the patient's condition has stabilized, where necessary by a specialized team. It assesses medical and psychosocial items and uses simple tests for the rapid detection of concomitant

diseases, an evaluation of the patient's autonomy and his/her social conditions. The SCGA makes it possible to evaluate frailty characterized by a reduction in physiological capacities to adapt to stress or changes in the environment associated or not with organ failure. The main items of the SCGA are the following.

Evaluation of cognition

The MMSE (Folstein's MMSE [12]), scored out of 30, constitutes a simple, rapid and standardized test for detecting cognitive impairment (Appendix 1) [13]. The threshold value depends on the patient's age and sociocultural level. A score over 27 is considered to be normal. A score below 24 is abnormal and dictates the need for a detailed assessment of cognitive function in a specialized unit. A score of between 24 and 27 should be considered abnormal for patients who are not extremely old (< 80 years), with a high sociocultural level and who have disturbances of memory or other cognitive functions. An abnormal MMSE score shows cognitive dysfunction not necessarily related to dementia. An abnormal score therefore calls for specialized evaluation and is not sufficient in itself to establish diagnosis.

Evaluation of dependence

Evaluation of dependence specifies limitations that may hinder complementary investigations, worsen prognosis [14] and impact the therapeutic approach. Dependence may be assessed with Activities of Daily Living scales (IADL or ADL) by interviewing the patient and his/her close contacts. There is a shortened four-item form of the IADL [15] based on: use of the telephone, means of transport, medication use and management of money (Appendix 2). The ADL scale provides information about personal hygiene, dressing, use of toilets, transferring, urine and bowel continence and eating. The subject is considered to be dependent as soon as he/she needs human help to carry out the activity concerned (Appendix 3) [16].

Somatic geriatric evaluation

This takes into account the evaluation of gait disorders and the risk of falling (unipedal stance test to evaluate the capacity to stand on one leg for 5 seconds). Likewise, nutritional status is assessed using validated scales (MNA scale) for the assay of plasma albumin or prealbumin [17]. Body weight must be interpreted after taking into account possible malnutrition and any fluid retention or dehydration.

Psychological evaluation

Depression is very frequent in older adults and may impact the manifestations of coronary disease and its treatment. It represents an independent risk factor for cardiovascular mortality [18]. Its detection and management are therefore essential in older adults. The simplified GDS provides an initial assessment (Appendix 4).

Evaluation of life circumstances

The purpose of this evaluation is to:

- estimate adherence to the proposed treatment. If the patient cannot manage his/her own treatment, it must be determined how (preparation, use of a tablet container) and by whom (family, domestic assistant, carer, nurse) it will be administered;
- specify the procedures for preparing food and meals;
- evaluate the patient's state of isolation and his/her access to different care services.

Community health management

It is important to evaluate the patient's social condition and take into account the role of caregivers (family relations or friends). This management involves informing and educating the patient's close contacts about the disease to make sure that he/she takes the medication and permit rapid detection of any change in symptoms and thresholds for the triggering of symptoms. This may require implementation of a home-help system. Different types of care and support are available including help to ensure personal hygiene from a nurse or nursing auxiliary, supply of medications (nurse), meals-on-wheels, domestic help (home helper) or care-giving (carer).

Depending on the SCGA data, the patient may be seen by a geriatrician in order to organize management and appropriate follow-up. Such management of the frail elderly has been shown to result in a significant reduction in mortality and admission to institutions [19].

Additional diagnostic and prognostic investigations

Electrocardiogram (ECG)

The ECG is rarely normal at baseline in older persons with coronary disease. Interpretation of repolarization is often hindered by the presence of left ventricular hypertrophy, electrical sequelae of infarction, a left bundle branch block, electrosystolic pacing, treatment by digitalis preparations or electrolyte disorders. The resting ECG may, however, be normal [20]. In this case, repeated recordings at short intervals and clinical and laboratory examinations should improve diagnosis. The ECG also provides prognostic information. For instance, the risk of coronary events is raised in the case of ST-segment depression greater than 1 mm [21].

Exercise ECG

An exercise ECG may rarely be performed in older adults who often have mobility disorders, joint pain, physical deconditioning and concomitant neurological, vascular or respiratory disorders [22]. No study of the sensitivity and specificity of the exercise test has been performed in the very elderly. Those evaluating its prognostic value gave contradictory results [23,24].

Myocardial perfusion scintigraphy

Myocardial perfusion scintigraphy, at rest or after dipyridamole or dobutamine stress, has a good sensitivity and specificity in subjects aged over 80 years for the detection of significant coronary stenosis [25] and the evaluation of the prognosis [26], although this examination is not always available.

Stress echocardiography

Stress echocardiography may also be proposed in the elderly. Physical exercise may be used as stress factor although pharmacological stress testing is more often performed because of functional limitations. The sensitivity and specificity of exertional echocardiography are similar to those in populations of younger patients [27]. After 75 years, dobutamine stress echocardiography is accompanied by an increased incidence of hypotension and ventricular arrhythmia [28].

Other evaluation procedures

The role of coronary computed tomography angiography and magnetic resonance imaging in the diagnosis of the coronary insufficiency is undergoing evaluation in older adults in particular, because of the renal risks related to iodine injection required for the computed tomography scan.

Other complementary examinations

Assays of blood glucose levels and a lipid assessment are useful for the evaluation of cardiovascular risk. Serum creatinine concentrations and creatinine clearance calculated with the Cockcroft-Gault formula are used to assess renal function. Impaired renal function, in particular when severe (clearance < 30 mL/min), is a factor of poor prognosis, increasing the risk of adverse drug events especially if coronary angiography is performed. Rehydration is essential before conducting this examination, as soon as the clearance is less than 60 mL/min.

Markers of ischaemia and myocardial necrosis

Assay of biomarkers of myocardial ischaemia (creatinine phosphokinase, troponin) contribute to the diagnosis and prognosis for patients with ACS. The procedures for using and interpreting the results of these assays are not affected by age, although the presence of macro creatine kinases, leading to false positives, is more frequent in elderly women [29]. In the case of severe renal insufficiency, a slight rise in troponin T may occur outside any ACS [30].

Coronary angiography

Coronary angiography is the reference diagnostic examination for the detection of coronary lesions. It has a higher morbidity and mortality rate in octogenarians. The indication for coronary angiography must therefore be established after evaluating the patient's conditions, mainly with respect to possible revascularization.

Medical treatment of ACS in the older subject

Definition

ACS [31] in older adults comprises:

- ST-segment elevation ACS: prolonged suggestive chest pain (> 20 minutes' duration) accompanied by persistent ST-segment elevation (or new left bundle branch block); increase in cardiac biomarkers (in particular troponin I or T) [32];
- non-ST-segment elevation ACS: prolonged suggestive chest pain or chest pain of recent onset (de novo angina) or worsening of angina generally accompanied by electrical modifications without persistent ST-segment elevation; increase in cardiac biomarkers (in particular troponin I or T) [33,34].

Lack of 'evidence-based' data

Older adults are under-represented in the main studies in ACS. More than half of the trials conducted between 1996 and 2000 included no patient aged over 75 years [28]. It is not therefore known if the algorithms and guidelines established with cohorts of younger patients are applicable to older subjects. Likewise, the best endpoint for use in this population with a reduced life expectancy is not known (mortality, cardiovascular events or quality of life?).

Medical management

The different epidemiological studies all underline the delayed management and under-utilization of medication in ACS. Compared with younger patients, those over 75 years are less often given beta-blockers, aspirin, clopidogrel, statins, thrombolysis (in the case of ST-segment elevation ACS) and glycoprotein IIb/IIIa antagonists [2—4]. Conversely, elderly subjects often receive more calcium antagonists and angiotensin-converting enzyme inhibitors [4], probably because of the increased prevalence of hypertension and heart failure. Likewise, increased use of LMWHs is observed despite the increased bleeding risk in this population.

The optimum medical management of older adults with ACS is not very different from that of younger subjects. However, the frailty of this population dictates the need for increased rigor in respecting contraindications, careful institution of the different therapeutic classes and monitoring for possible side-effects.

Platelet-aggregation inhibitors

Aspirin

The prescription of aspirin is recommended [35,36] from the acute phase, at a dosage of between 75 and 325 mg/day in the absence of allergy, exacerbation of peptic ulcer or bleeding disorders, and must be continued over the long term. Its side-effects (mainly gastrointestinal) are uncommon at low doses (75—150 mg/day) but must be carefully sought.

Clopidogrel

The prescription of clopidogrel monotherapy is recommended in the case of contraindications to aspirin. The combination of clopidogrel with low doses of aspirin has not been evaluated in subjects over 80 years. Taking into account the divergent results of the CURE [37] and PCI-CURE studies [38] in patients aged over 65 years, dual antiplatelet therapy may only be recommended on an individual basis after taking into account the benefit-to-risk ratio for each patient.

The optimum duration of treatment with the aspirin—clopidogrel combination has not been well evaluated in older adults, and must take into account the patient's general status and/or the implantation of a drug-eluting stent. There are no data evaluating the benefit and safety of loading doses in patients over 80 years.

Withdrawal of antiplatelet therapy in older adults

This is frequently necessary because of the multiple comorbid diseases in this population. Discontinuation of platelet aggregation inhibitors is a major risk factor for thrombosis of all coronary stents and in particular late thrombosis in drug-eluting stents. Recommendations exist about the management of oral antiplatelet therapy in patients with coronary stents, in particular in patients requiring surgery, although these do not specifically concern elderly patients [39].

Glycoprotein IIb/IIIa antagonists

Few randomized studies have evaluated the benefit of glycoprotein IIb/IIIa antagonists in patients over 75 years. In patients with ST-segment elevation ACS, they may be used in primary angioplasty with coronary stenting [29,40] after careful analysis of the trade-off between benefit and risks, and ruling out contraindications (stroke, surgery or recent trauma, coagulation disorders, hepatic insufficiency, active haemorrhage, severe arterial hypertension). On the contrary, their prescription, in combination with fibrinolytics, is clearly contraindicated in patients over 75 years [29].

Subjects over 75 years, admitted for non-ST-segment elevation ACS also seem to benefit from adjunctive anti-glycoprotein IIb/IIIa therapy with early revascularization at the price, however, of increased bleeding [41].

Anticoagulants

Unfractionated heparin

Unfractionated heparin is recommended in ST-segment elevation ACS whatever revascularization procedure is used, provided there are no immunoallergic or haemorrhagic contraindications [42]. In subjects aged over 75 years with ST-segment elevation ACS undergoing treatment with fibrinolysis, unfractionated heparin was better tolerated than the LMWH enoxaparin in terms of the risk of intracranial haemorrhage [37]. In these high-risk patients, clinical and laboratory monitoring should be reinforced for signs of visceral or cerebral bleeding.

Low molecular weight heparin

LMWHs, in particular enoxaparin, are recommended in young patients with ACS [43]. After the age of 75 years, in combination with thrombolysis during the acute phase of myocardial infarction, a subgroup of the ASSENT-3 study suggested that LMWH and unfractionated heparin had similar benefits in terms of the composite endpoint of death, in-hospital reinfarction, refractory ischaemia, intracranial haemorrhage and major bleeding [44]. However, the risk of intracranial haemorrhage was higher with enoxaparin than with unfractionated heparin in older adults in ASSENT-3 Plus [42].

The advantages of LMWH are their ease of use and the lower risk of heparin-induced thrombocytopenia compared with unfractionated heparin. Conversely, they must be prescribed with caution in patients aged over 75 years because of their renal elimination. The dosage must be adjusted according to renal function and anti-Xa activity to avoid accumulation responsible for haemorrhagic accidents [45]. A creatinine clearance less than 30 mL/min is an absolute contraindication for curative doses whereas a clearance of between 30 and 60 mL/min is a relative contraindication (with obligatory control of anti-Xa activity). The duration of anticoagulant treatment ranged from 48 hours to eight days depending on the studies and the type of revascularization procedure which is not codified in the elderly.

Direct antithrombotics and factor Xa inhibitors

Although they are not currently recommended in elderly patients with ACS [36], direct thrombin inhibitors appear promising [46,47]: fondaparinux appears to have a similar efficacy to that of enoxaparin in patients with non-ST-segment elevation ACS, with a lower bleeding risk, particularly in older subjects [48]. In ST-segment elevation ACS, although safety was the same, the benefit was not as marked as in the subgroup of patients undergoing primary angioplasty [49].

Vitamin K antagonists

Vitamin K antagonists are not part of the treatment armamentarium in ACS. They must be stopped where necessary and relayed by heparin anticoagulation.

Beta-blockers

Irrespective of the type of ACS (ST-segment elevation or non-ST-segment elevation), beta-blockers have clear short- and long-term benefits in terms of reducing recurrence of myocardial infarction and increasing survival. Although few studies have included patients over 75 years, the data obtained from meta-analyses and registries show a benefit whatever the patient's age. They are recommended for first-line treatment [29], in particular in the case of left ventricular dysfunction [50] after ruling out all the usual contraindications, such as decompensated heart failure, asthma and advanced chronic obstructive pulmonary disease, and severe conduction disorders, which must be sought with particular care in the elderly.

Close monitoring of blood pressure, heart rate and the ECG are necessary in this setting. Monitoring for the onset of bradycardia is necessary in the case of concomitant prescription of acetylcholinesterase inhibitors. Institution of beta-blockers must be delayed if there are overt signs of water and sodium retention. Treatment should be initiated cautiously with gradual up-titration of the dose to a target resting heart rate of approximately 60 beats per minute.

Inhibitors of the renin-angiotensin system

Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are recommended during the first 24 hours of onset of ACS if there are clinical signs of heart failure and/or a deterioration

in left ventricular systolic function (left ventricular ejection fraction < 40%) and/or anterior-wall infarction [51,52]. They are indicated after myocardial infarction in all patients and indefinitely, in the absence of contraindications. There are few data specific to patients aged over 75 years and these concern subgroup analysis [53]. ACE inhibitors should be initiated cautiously in older adults and the dose gradually increased according to renal function. In general, the daily dosage should be reduced by half compared with that used in younger patients. Treatment should be initiated long after any episode of sodium depletion, starting with a low dosage, which is then gradually up-titrated to the maximum tolerated dose. At the same time, the continuation or interruption of other therapies such as diuretics, calcium antagonists and nitrates should be re-evaluated. Prescription of non-steroidal anti-inflammatory drugs is contraindicated because of the risk of renal insufficiency and hyperkalaemia. Blood pressure (seated and standing), renal function and blood electrolytes must be monitored carefully and very regularly during the first months after myocardial infarction, and systematically in the case of acute intercurrent episodes of fever, diarrhoea, dehydration, vomiting, etc.

Angiotensin II receptor antagonists (ARAs)

Two trials [54,55] evaluated the role of ARAs in post-infarction heart failure, and included a significant number of patients aged over 75 years. The results showed that ARAs had a similar efficacy to ACE inhibitors irrespective of the patient's age. Their use is therefore restricted to post-infarct patients intolerant to ACE inhibitors and younger subjects. They must be instituted at a low dose. Upward dose titration and monitoring procedures are similar to those recommended for ACE inhibitors.

Aldosterone antagonists

No significant differences in benefit were observed between different age groups when eplerenone was used post-infarction in patients with signs of heart failure or left ventricular dysfunction. The chosen threshold was, however, particularly low (65 years) [56]. Because of the risk of hyperkalaemia due to renal function impairment in the elderly, the trade-off between risks and benefit should be carefully assessed and the contraindications respected in the absence of any specific study.

Statins

Few scientific data are available showing the benefit of statins administered to ACS patients aged over 75 years. However, subgroup studies suggest that their beneficial effect is at least the same as that obtained in younger patients [57]. The target low-density lipoprotein cholesterol value and the doses required to reach it have not been determined.

Calcium antagonists

Dihydropyridines have not been shown to have any benefit in patients with an ACS. They should only be prescribed within the scope of their recognised indications, such as hypertension. They are not therefore recommended except in the specific case of confirmed coronary spasm.

The use of rate-limiting calcium antagonists (diltiazem, verapamil) may be considered when beta-blockers are contraindicated, with strict monitoring of the heart rate, ECG and blood pressure and for the possible onset of signs of heart failure.

Nitrates

Nitrates have not been shown to improve outcomes in patients with ACS [58,59]. However, in the subgroup of patients aged over 70 years included in GISSI-3, nitrates administered within 24 hours of the onset of myocardial infarction significantly reduced cardiovascular complications [59].

They may be particularly useful in subgroups of ACS patients with recurrent or persistent myocardial ischaemia and/or left ventricular insufficiency and/or exacerbations of their high blood pressure [5]. They may be used temporarily at low doses to relieve pain, in the absence of hypotension or right ventricular infarction and with close monitoring of blood pressure and for the onset of headaches.

Potassium channel agonists

No data are available in older adults with ACS. This treatment may, however, be considered in the case of clinically persistent angina if blood pressure values allow after the institution of the other pharmacological classes.

Myocardial revascularization

Coronary reperfusion for myocardial infarction in older adults remains a controversial subject, mainly because of the under-representation or even exclusion of patients aged over 75 years in large clinical trials [60—62].

Intravenous thrombolysis in myocardial infarction in older adults

Several studies and registries have underlined the increased risk of haemorrhage with advancing age during the hospital phase [63,64]. Nevertheless, thrombolysis significantly reduces 1-year mortality in patients over 75 years of age [65,66].

The risk of cerebral haemorrhage is twice as high after the age of 85 years but remains acceptable (approximately 3%) [67]. Factors predisposing to bleeding are: age, presence of comorbidities, malnutrition, severe arterial hypertension and brain trauma.

Coronary angioplasty

The results of a recent meta-analysis of randomized trials [68] show that angioplasty in patients aged over 80 years has a greater benefit than thrombolysis, with, in particular, a better survival and a lower risk of stroke. These conclusions are coherent with those of observational studies [69—72]. This management strategy avoids the risks of haemorrhage due to thrombolysis. However, in older adults, angioplasty

is accompanied by a risk of more severe complications than in younger individuals (deaths, renal insufficiency, vascular complications) [73]. An evaluation of renal function before and after angioplasty is essential. It is particularly important to apply preventive measures with adequate hydration in the case of renal insufficiency. The indications for angioplasty during the acute phase in older adults must therefore be taken into account:

- clinical severity (recurrence of pain, heart failure);
- severity of the ischaemia (anterior territory or extension to the right ventricle, large rise in troponin);
- delay after the onset of signs (< 6 hours);
- physiological status (life expectancy, quality of life);
- presence of comorbidities (renal insufficiency, cognitive disorders, dependence, etc.).

Coronary angioplasty with or without stent implantation

No randomized study has compared angioplasty with or without stenting in the very elderly subject with myocardial infarction.

Revascularization in the case of cardiogenic shock

According to the SHOCK study, irrespective of the revascularization strategy (angioplasty or bypass) a reduction in mortality at six months is observed only in those aged under 75 years [74]. However, certain studies suggest a benefit on mortality after early revascularization in elderly patients selected according to individual criteria [75—77]. Revascularization, in this setting, can only be decided at the end of an individual decision process.

Coronary artery bypass grafting

The perioperative morbidity and mortality of bypass grafting increase in older adults more especially if they have unstable angina or require emergency surgery [78,79].

Summary

Angioplasty may be considered to be the technique of choice for emergency reperfusion. However, if this technique cannot be used, thrombolysis has benefits that should entail its wider use when the patient's physiological status permits.

Treatment of chronic coronary disease

Medication for chronic ischaemic heart disease in older adults comprises two aspects:

- symptomatic treatments to reduce the frequency of angina pain and improve tolerance to exercise: nitrates, beta-blockers, calcium channel blockers, molsidomine, nicorandil, trimetazidine and ivabradine;
- secondary preventive treatments to improve outcomes by reducing morbidity and mortality: beta-blockers, aspirin, clopidogrel, statins, ACE inhibitors and ARAs.

Treatment of angina attacks

For exertional angina, sublingual nitrates remain the basic treatment to relieve pain. The risk of orthostatic hypotension after nitrate administration is increased in older adults, especially in the presence of aortic stenosis. They must be taken while seated. The elderly subject must receive advice about the factors precipitating angina attacks, how to take glyceryl trinitrate and the recommended treatment for intractable pain. The patient and his/her close relations must understand this information.

Symptomatic treatment of stable angina pectoris

Few data are available in the literature about the antiangina efficacy of the different therapeutic classes in older adults. The conclusions of trials in the general population have therefore been extrapolated to the elderly [80].

Beta-blockers

The use of beta-blockers is recommended in the absence of contraindications. Beta-blockers reduce the frequency of angina attacks and episodes of silent ischaemia [81,82]. Their dosage must be adjusted to maintain a resting heart rate of about 60 beats per minute and reduce the acceleration of heart rate during exercise [20,83]. Their administration should respect the precautions for use described in the section on ACS. A beta-1 selective beta-blocker should be preferred in patients with chronic and stable lower-limb arterial disease or diabetes. It is recommended not to suddenly discontinue beta-blocker treatment in patients with angina because of the increased risk of infarction and sudden death [84].

Calcium antagonists

Calcium channel blockers, indicated in stable chronic angina, have a similar antiangina efficacy as beta-blockers [85]. The use of the rate-limiting calcium antagonists (diltiazem, verapamil) in older adults is contraindicated in the case of decompensated heart failure, severe conduction disorders and beta-blocker administration.

Long-acting nitrates

Long-acting nitrates reduce the frequency and severity of angina attacks. No placebo-controlled study has been performed showing that nitrates have a benefit on morbidity and mortality. They reduce the frequency and severity of angina attacks, but in older adults they are also one of the main therapeutic classes responsible for orthostatic hypotension. They may be used in the case of contraindication or poor tolerability of beta-blockers and calcium antagonists [82]. Tight aortic stenosis and obstructive cardiomyopathy are contraindications to the use of nitrates.

Other antiangina agents: molsidomine, nicorandil, trimetazidine, ivabradine

Molsidomine is a nitric-oxide donor with similar effects to nitrates. Nicorandil is a potassium channel activator with a vasodilator effect with similar effects to nitrates. The IONA [86] study showed a benefit for hospital readmissions for angina, but did not include very elderly subjects. These

two products may be used as an alternative to nitrates when these are poorly tolerated.

Trimetazidine is a metabolic antiangina drug that inhibits the beta-oxidation of fatty acids by mitochondria. It has not been shown to have an effect on prognosis [87].

The role of new heart-rate-lowering antiangina agents that inhibit the I(f) current, such as ivabradine, is not currently codified in very elderly subjects as no specific study has been performed in this population. Symptomatic treatment must be reassessed regularly and may be reduced if angina attacks become rare.

Secondary prevention

As in younger patients, the secondary prevention of coronary events in older adults is based on the use of antithrombotic agents, beta-blockers, ACE inhibitors/ARAs and statins, and on the control of blood pressure, in combination with diet and lifestyle measures.

Antiplatelet therapy

Treatment with platelet-aggregation inhibitors is indicated in older adults for the secondary prevention of myocardial infarction. Treatment must be continued indefinitely in the absence of haemorrhagic complications. The inhibition of platelet aggregation by aspirin effectively prevents the recurrence of myocardial infarction and cardiovascular mortality. The Antiplatelet Trialists Collaboration [88] meta-analysis showed a 27% reduction in cardiovascular complications (infarction, stroke and death from vascular causes) with aspirin. This benefit was observed irrespective of age group (> or < 65 years). Clopidogrel has proven efficacy for the prophylaxis of myocardial infarction in the over 65 subgroup of patients at high cardiovascular risk [89].

Beta-blockers, ACE inhibitors and ARAs

The dosages of beta-blockers and inhibitors of the renin-angiotensin system must be adjusted according to their safety, and treatment continued indefinitely. Monitoring procedures are the same as during the acute phase.

Beta-blockers are recommended for the secondary prevention of myocardial infarction. Their administration reduces the risk of death in older adults who have survived myocardial infarction [90]. ACE inhibitors are also recommended for the secondary prevention of myocardial infarction in the elderly provided that they are well tolerated (in particular with respect to blood pressure and renal parameters). They are effective after myocardial infarction, with [52,91,92] or without left ventricular dysfunction [93—96] to reduce the risk of mortality and cardiovascular events. This benefit is similar whatever the age (< or > 65 years [82,85]), although these studies did not include very elderly patients.

ARAs had a similar benefit to that observed with ACE inhibitors in post-infarction complicated by heart failure or left ventricular dysfunction and in patients with coronary disease [55,97]. They may therefore be used in patients intolerant to ACE inhibitors.

Statins

Statins are recommended for the secondary prevention of myocardial infarction in older adults. They effectively prevent coronary events in elderly subjects at high cardiovascular risk. The PROSPER study [98], which included patients aged 70 to 82 years, showed that pravastatin significantly reduced the risk of death from coronary artery disease. In the Heart Protection Study [99], which included more than 5000 patients over 75 years of age with arterial disease, cerebrovascular disease or diabetes, simvastatin reduced the incidence of a first non-fatal episode of myocardial infarction or death from coronary disease. The risk reduction was similar whatever the age. Lastly, a recent meta-analysis showed a 22% reduction in 5-year mortality in patients over 65 years receiving statins for secondary prevention [100].

Antihypertensive medication

Antihypertensive medications effectively reduce the incidence of myocardial infarction in hypertensive subjects aged 60 to 80 years, with a risk reduction of 20—30% [101]. In patients aged over 80 years, the HYVET study showed a benefit of treatment with thiazide diuretic (indapamide) with or without an ACE inhibitor, with a 34% reduction in cardiovascular events [102]. In this study, the 28% reduction in myocardial infarction observed with treatment was found to be non-significant, possibly because of the lack of statistical power after premature discontinuation of the study.

Lifestyle changes

Smoking cessation has a positive impact on the outcome of coronary artery disease, including in elderly subjects. Smoking cessation after myocardial infarction reduces mortality by 25—50% [103], regardless of age. Smoking cessation is possible in older adults and is achieved at rates equivalent to or higher than those observed in younger subjects.

Physical exercise and rehabilitation

In the general population, controlled trials have demonstrated the benefit of rehabilitation in terms of functional capacities, mortality [104], reduction in atherosclerosis lesions [105] and in the number of hospital admissions for a coronary event [106]. The impact of rehabilitation in older adults was not specifically evaluated.

Rehabilitation also leads to an improvement in performance of the ADL [107]. Besides aerobic rehabilitation, resistance-training techniques (anaerobic) are effective in the elderly [108—110]. Exercises performed at home are as well tolerated and as effective as exercises performed in rehabilitation centres with medical monitoring [111].

Management of excess body weight

Obesity is a traditional risk factor for coronary artery disease, including in the elderly [112,113]. Body mass index should be calculated in all coronary patients [114]. However, in the case of malnutrition, body mass index [115] cannot be used to recognize sarcopenic obesity (obesity with

weight loss due to loss of muscle mass), which is particularly frequent in older subjects.

As no interventional study has yet been performed, the dietetic procedures required to reduce cardiovascular risk in overweight older adults do not form the subject of a consensus. In overweight, elderly coronary patients a small reduction (500 to 700 kcal/j) in energy intake may be proposed while maintaining a daily protein intake of 1 g/kg per day in order to achieve a weight loss of 8—10% in six months [116]. Conversely, too great a weight loss in an elderly patient may have a negative effect by decreasing the muscle mass and protein reserve. Regular physical activity may increase weight loss without leading to muscle loss and should be widely recommended in elderly subjects.

Myocardial revascularization

The type of myocardial revascularization (angioplasty or surgery) performed in older adults depends on clinical criteria (comorbidities, clinical severity) and paraclinical parameters (documented myocardial ischaemia, left ventricular function, angiographic appearance of coronary lesions). A case-by-case evaluation is necessary in these patients in order to evaluate the benefit-risk ratio.

Coronary angioplasty

Angioplasty allows rapid treatment of coronary lesions compared with surgery, which generally requires extracorporeal circulation. Long hospital stays generating complications specific to this type of patient are therefore avoided. However, in older adults the coronary arteries needing revascularization are often the site of particularly complex lesions (extensive, diffuse, calcified lesions with frequent stenosis of the left main trunk and chronic coronary occlusions) [117].

Primary success rates vary between 80 and 96%, but revascularization is generally incomplete in patients aged over 75 years [118], with a history of infarction [119], with calcified total or sub-total coronary occlusion [120], or in the case of involvement of the circumflex artery [121].

The technical difficulties of PTCA place elderly patients in a high-risk group for per- and post-procedure complications [122—125].

Although the in-hospital complication rates and mortality are low, they are slightly higher than those of a younger population (2—3%). After 65 years of age, in-hospital mortality is independently associated with a left ventricular ejection fraction less than 40%, the existence of triple-vessel lesions and with female gender [126]. Medium-term mortality after successful PTCA is not increased in older adults [127]. Compared with the medical strategy, PTCA has no benefit on mortality or on the recurrence of major cardiovascular events, but improves quality of life [128,129].

The indications for stenting in older adults are the same as in younger patients. The benefit compared with PTCA alone is not documented in patients aged over 80 years. The risk of bleeding induced by dual antiplatelet therapy should be carefully assessed before implanting a drug-eluting stent.

Coronary artery bypass grafting

The benefit of surgery on survival has been demonstrated in older adults but few studies have included patients aged over 80 years [130]. Coronary artery bypass grafting has a high risk of complications (stroke, cognitive impairment, bleeding, respiratory decompensation), of approximately 30% in octogenarians [78,131].

The main predictive factors of mortality are an elderly age, female gender, resting angina, diabetes, left ventricular ejection fraction less than 40%, heart failure, renal insufficiency and emergency surgery [132]. In this setting, the appropriateness of surgical revascularization should be carefully considered by taking into account in particular the risk of deterioration of cognitive function observed after a surgical procedure.

The use of scores, such as EuroSCORE [133,134], may help to evaluate the risk of postoperative mortality, taking into account patient-related parameters (age, comorbidities), cardiopathy (left ventricular ejection fraction, unstable angina) and the surgical procedure (emergency surgery, concomitant non-coronary surgery, surgery of the chest aorta, septal rupture).

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Appendix 1. Mini Mental State Examination (MMSE)

Reference: Derouesne C, Poitreneau J, Hugonot L, Kalafat M, Dubois B, Laurent B. Mini-Mental State Examination: a useful method for the evaluation of the cognitive status of patients by the clinician. Consensual French version. Presse Med 1999;28:1141—8.

Orientation

I am going to ask you a few questions to assess how well your memory works. Some are very simple, others are less so. Please answer as best you can.

Score/5 ☐

1. What is the year? ..... ☐
2. What is the season? ..... ☐
3. What is the month? ..... ☐
4. What is the day of the month(date)?..... ☐
5. What is the day of the week? ..... ☐

I am now going to ask you a few questions about the place where we are at the moment:

Score/5 ☐

6. What is the name of the hospital we are in(if the examination is conducted at the office, asking the name of the street)? ..... ☐
7. In which town is it? ..... ☐
8. In which *department* (county) is this town located? ☐
9. In which region is this *department*? ..... ☐
10. What floor are we on? ..... ☐

Learning

I am going to say 3 words. I want you to repeat them to me and try and remember them because I will ask you again later.

Score/3 ☐

11. Cigar ..... ☐
12. Flower ..... ☐
13. Door ..... ☐

Repeat the 3 words.

Attention and calculation

Count backwards from 100 by subtracting 7 each time

Score/5 ☐

14. 93 ..... ☐
15. 86 ..... ☐
16. 79..... ☐
17. 72 ..... ☐
18. 65 ..... ☐

For all subjects, even those with the maximum points, ask: Please spell the word *MONDE* backwards: EDNOM.

The score is the number of letters in the right place. (This figure must <u>not</u> appear in the global score.)

Recall

Can you tell me the 3 words that I asked you to repeat and remember a few moments ago?

Score/3 ☐

19. Cigar ..... ☐
20. Flower ..... ☐
21. Door ..... ☐

Language

Score/9 ☐

22. Show the patient a pencil. *What is this called?* ..... ☐
23. Show your watch. *What is this called?* ..... ☐
24. *Listen carefully and repeat after me: "No ifs, ands or buts"* ..... ☐

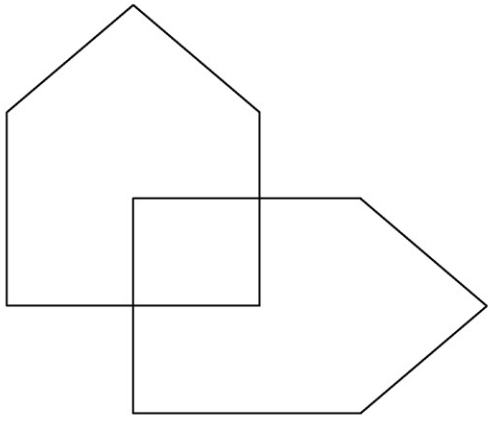
25. Place a sheet of paper on the desk and show it to the subject while saying: *Listen carefully and do what I tell you to do:*
    Take this paper sheet with the right hand, ... ☐
26. Fold it in half ..... ☐
27. And throw it on the floor ..... ☐

28. Give the subject a sheet of paper with the following written in large letters: **"Close your eyes"** and tell the subject:
    Do what it says ..... ☐

29. Give the subject a sheet of paper and a pen and tell the patient: *Write any sentence that you want though it must be a whole sentence.* This sentence must be written spontaneously. It must contain a subject, a verb and make sense. ☐

Copying

30. Give the subject a sheet of paper and ask him or her:
    "Can you copy this drawing?" ☐



Score total (0 to 30) :
NORMAL SCORE = 25 ± 2

Appendix 2. Simplified IADL Scale (PAQUID Study)

Reference: Barberger-Gateau P, Dartigues JF, Letenneur L. Four Instrumental Activities of Daily Living Score as a predictor of one-year incident dementia. Age Ageing 1993;22:457—63.

1. **Ability to use the telephone**
   - ☐ Makes use normally of the telephone (telephones on his/her own initiative, composes numbers)

2. **Means of transport**
   - ☐ Uses public transport independently or drives his/her own car

3. **Responsibility for own medications**
   - ☐ Deals with his/her own medications personally (correct doses and schedules)

4. **Ability to handle finances**
   - ☐ Manages his or her budget autonomously (writes cheques, pays the rent and bills, bank operations)

Each of the 4 items scored (0) = need for help, (1) = no need for help, according to the response.

Score/4 ☐

(normal score = 4/4)

Appendix 3. Katz ADL Scale

Reference: Katz A, Ford AB, Moskowitz RW et al. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. J Am Med Assoc 1963;185:914—9

Bathing (wash-basin, bath or shower and body hygiene)
1 ☐ No need for help
½ ☐ Partial need for help
0 ☐ Dependence

Dressing (gets clothes from cupboards or drawers, including underwear and outer garments and uses button and zip fasteners)
1 ☐ No need for help
½ ☐ Autonomous for the choice of clothes and getting dressed but may need help tying shoes
0 ☐ Dependence

Toileting (to urinate or defecate, wipe themselves and get dressed)
1 ☐ No need for help
½ ☐ Must be accompanied or needs help to undress and put clothes back on
0 ☐ Can't go to the toilets alone or doesn't use the bedpan

Transferring
1 ☐ Moves in and out of bed or chair unassisted (may use a stick or walker)
½ ☐ Needs help
0 ☐ Stays in bed (bedridden)

Continence
1 ☐ Complete self control over urination and defecation
½ ☐ Occasional accidents
0 ☐ Completely incontinent

Feeding
1 ☐ No need for help
½ ☐ Needs help cutting meat, buttering bread or peeling fruit
0 ☐ Needs total help with feeding

Score/6 ☐

(Normal score = 6/6)

Appendix 4. Mini GDS (Geriatric Depression Scale), mood assessment

Reference: Clément J-P, Nassif RF, Leger JM, Marchan F. Mise au point et contribution à la validation d'une version française brève de la Geriatric Depression Scale de Yesavage. L'Encéphale 1997;XXIII:91—9.

Ask the patient to answer the questions by saying how he/she has felt during the last week and not during his life or at the present time.

1. Do you often feel discouraged and sad?	yes = 1, no = 0
2. Do you feel that your life is empty?	yes = 1, no = 0
3. Are you happy most of the time?	yes = 0, no = 1
4. Do you have the impression that your situation is desperate?	yes = 1, no = 0

Score

If total score equal or greater than 1, strong probability of depression

If total score = 0, strong probability of no depression

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